

## **ANDA 200652**

# **Alosetron Tablets**

Selective 5-HT<sub>3</sub> antagonist

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## **RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

### **I. GOALS:**

- To mitigate the risk of ischemic colitis (IC) and serious complications of constipation (CoC) associated with alosetron hydrochloride (hereinafter, referred to as alosetron) by ensuring that alosetron is used in only severely affected patients for whom benefits exceed the risks.
- To ensure that the risk of IC and serious CoC with the use of alosetron are communicated to patients, pharmacists, and prescribers.

### **II. REMS ELEMENTS:**

#### **A. Medication Guide**

A Medication Guide for alosetron will be dispensed with each alosetron prescription in accordance with 21 CFR 208.24. A Medication Guide will be dispensed with each 30-tablet bottle (typical dispense is 2 bottles per month). Copies of the Medication Guide will be available on the Alosetron REMS website at [www.AlosetronREMS.com](http://www.AlosetronREMS.com) or via the Alosetron REMS contact center at 1-844-267-8675.

Additionally, as part of the REMS program for alosetron, a copy of the Medication Guide will be provided to certified prescribers who will provide a Medication Guide to each patient at the initiation of each new course of alosetron therapy.

## **B. Elements to Assure Safe Use**

### **1. Healthcare providers who prescribe alosetron will be specially certified.**

- a. Roxane Laboratories (Roxane) will ensure that healthcare providers who prescribe alosetron are specially certified in the Alosetron REMS Program. To become certified, each prescriber of alosetron enrolls in the Alosetron REMS Program by submitting a completed Alosetron REMS Program Prescriber Enrollment Form and attesting to the following:
  - i. I request to participate in the Alosetron REMS Program and acknowledge that I have read and understand the complete Prescribing Information and other enrollment materials for the Alosetron REMS Program. I understand the risks associated with its use and will follow the requirements of the Alosetron REMS Program described below. I understand the importance of reporting all cases of ischemic colitis and serious complications of constipation to the Alosetron REMS Program at 1-844-267-8675.
  - ii. I understand that alosetron is approved only for women with severe, diarrhea-predominant irritable bowel syndrome who have:
    - chronic irritable bowel syndrome symptoms (generally lasting for 6 months or longer),
    - had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and
    - not responded adequately to conventional therapy.

Diarrhea-predominant irritable bowel syndrome is severe if it includes diarrhea and one or more of the following:

- frequent and severe abdominal pain and discomfort,
  - frequent bowel urgency or fecal incontinence
  - disability or restriction of daily activities due to irritable bowel syndrome.
- iii. I understand that if I prescribe alosetron for my patient(s), I must be able to perform the following:

- Diagnose and manage irritable bowel syndrome, ischemic colitis, constipation, and complications of constipation or refer patients to a specialist as needed.
- Ensure that all patients under my care are educated by me or a healthcare provider in my practice about the benefits and risks of the drug.

iv. I agree to:

- provide each of my patients with a copy of the Alosetron Medication Guide at initiation of alosetron treatment.
- review the content of the Medication Guide and encourage the patient to read it and ask questions.
- have each patient sign the Alosetron Patient Acknowledgement Form. The original signed form must be placed in the patient's medical record, and a copy given to the patient.
- inform my patients about the Alosetron Patient Follow-Up Survey, encourage them to participate and provide them with an Alosetron Patient Follow-Up Survey Pre-Enrollment Form.
- affix Alosetron REMS Program stickers to written prescriptions for alosetron (i.e., the original and all subsequent prescriptions). Alosetron REMS stickers will be provided as part of the Alosetron REMS Program. Refills are permitted to be written on prescriptions.
- ensure that all prescriptions for alosetron are written and not transmitted by telephone, facsimile, or computer.

- Alosetron REMS Program materials can be requested via the Alosetron REMS Program website at [www.AlosetronREMS.com](http://www.AlosetronREMS.com) or by phone at 1-844-267-8675.
- Roxane will provide prescribers an Alosetron REMS Program Kit upon their enrollment.
- Roxane will maintain a database of all certified enrolled alosetron prescribers.

The following materials are part of the Alosetron REMS Program and are appended:

- Alosetron REMS Program Prescriber Enrollment Materials:
  - Alosetron REMS Program Enrollment Letter
  - Alosetron REMS Program Prescriber Enrollment Form
  - Alosetron REMS Program Prescriber Education Slide Deck
  - Alosetron Prescribing Information and Alosetron Medication Guide

- Alosetron REMS website for the Prescriber Section web screen shots
- Alosetron REMS Program Kit:
  - Alosetron REMS Program Kit Overview Letter
  - Alosetron REMS Program Patient Acknowledgement Form
  - Alosetron Prescribing Information and Alosetron Medication Guide
  - Alosetron REMS stickers
  - Alosetron REMS Program Patient Follow-Up Survey Pre-Enrollment Form

**2. Each patient prescribed alosetron must have signed an Alosetron REMS Program Patient Acknowledgment Form for documentation of safe-use conditions. By signing the Alosetron REMS Program Patient Acknowledgment Form, the patient agrees to the following:**

- a. My doctor or healthcare provider under a doctor's direction, answered my questions about treatment with alosetron. I have read and I understand the Medication Guide for alosetron, including the section "Who should not take alosetron?" I understand that about 1 out of every 1,000 women who take alosetron may get serious complications of constipation. I understand that about 3 of every 1,000 women who take alosetron over a 6-month period may get a serious problem where blood flow to parts of the large bowel is reduced (ischemic colitis). I understand that the serious condition of ischemic colitis, and other serious complications of constipation, can happen suddenly. These serious complications may lead to a hospital stay, and in rare cases, blood transfusions, surgery, and death.
- b. I understand that certain people may be more likely to develop a serious bowel condition while taking alosetron, including people who:
  - are older,
  - have other health problems,
  - take other medicines that may cause constipation.
- c. I understand alosetron is a medicine that should only be used for some women with severe chronic irritable bowel syndrome (IBS), whose main problem is diarrhea, and whose IBS symptoms have not been helped enough by other treatments.
- d. I will follow instructions in the Alosetron Medication Guide about:
  - **telling my doctor**, before taking alosetron, about any illnesses I have, or other medicines I am taking or planning to take.
  - **taking alosetron** exactly as my doctor prescribes it.

- **stopping alosetron** and calling my doctor right away if I get constipated, if I have new or worse pain in my stomach area (abdomen), or if I see blood in my bowel movements.
  - **calling my doctor** again if the constipation I called about before has not gotten better.
  - **not starting alosetron again** unless my doctor tells me to do so, if I stopped taking it because I got constipated.
  - **talking with my doctor 4 weeks after starting alosetron** to recheck my IBS symptoms.
  - **stopping alosetron and calling my doctor** if my IBS symptoms have not improved after 4 weeks of taking 1 mg alosetron 2 times a day.
- e. If I see other doctors about my IBS or possible side effects from alosetron, I will tell the doctor who prescribed alosetron.

The following materials are part of the Alosetron REMS Program and are appended.

- Alosetron REMS Program Patient Acknowledgement Form
- Alosetron REMS website for Patients web screen shots
- Alosetron Medication Guide

### **3. Pharmacists will only dispense alosetron to patients with documentation of safe-use conditions:**

- a. The pharmacists will only dispense a prescription for alosetron in the presence of an Alosetron REMS sticker.<sup>1</sup>

The Alosetron REMS sticker provides verification to the pharmacist that the prescription is written by a certified prescriber enrolled in the Alosetron REMS Program.

Pharmacists will not accept telephone, facsimile, or computerized prescriptions for alosetron. The prescription may provide refills (30-day supplies).

- b. At the time of filling the prescription, pharmacists will dispense to the patient a 30-day supply which includes a copy of the Alosetron Medication Guide.

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<sup>1</sup> In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitution of alosetron is permitted pursuant to State substitution laws.

- c. Roxane will perform educational mailings to pharmacists and retail pharmacies using an Alosetron Dear Pharmacist Letter at least 2 weeks prior to first availability of the Alosetron REMS Program and annually thereafter. The mailings will remind the pharmacists about their role within the Alosetron REMS Program.
- d. Roxane will direct pharmacists to review educational materials on the pharmacist section of the Alosetron REMS Program website. The educational materials will consist of the Alosetron REMS Program Pharmacist Education Slide Deck, discussing the benefits and risks of alosetron therapy and the pharmacist role in ensuring compliance with the REMS sticker program.

The following materials are part of the REMS and are appended:

- Alosetron Dear Pharmacist Letter
- Alosetron REMS Program Pharmacist Education Slide Deck
- Alosetron REMS website for Pharmacists Section web screen shots

## **C. Implementation System**

The implementation system for the Alosetron REMS Program includes the following:

1. Roxane will monitor compliance with completion of the Alosetron REMS Program Prescriber Enrollment Form and the Alosetron REMS Program Patient Acknowledgement Form to help ensure alosetron is prescribed by Alosetron REMS Program-enrolled prescribers and that patients are only treated with alosetron following documentation of safe-use conditions by conducting surveys of prescribers and patients.
2. Roxane will monitor compliance with the REMS program sticker by conducting surveys of pharmacists, prescribers, and patients to help ensure alosetron prescriptions are written by Alosetron REMS Program-enrolled prescribers and dispensed by pharmacists in accordance with the requirements of the Alosetron REMS Program.
3. Based on monitoring and evaluation of the elements to assure safe use in section, II.B., Roxane will take reasonable steps to improve the implementation of these elements, if found to be inadequate, and to address non-compliance with the requirements of the Alosetron REMS Program.